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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/800,291	03/12/2004	Zoltan G. Toth	14669.0064USU1	8286

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Merchant & Gould
P.O. Box 2903
Minneapolis, MN 55402-0903

EXAMINER	
SCHLIENTZ, NATHAN W	
ART UNIT	**PAPER NUMBER**
1616	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/800,291	TOTH ET AL.	
	Examiner	Art Unit	
	Nathan W. Schlientz	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-60* is/are pending in the application.

4a) Of the above claim(s) *14,27 and 60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,15-26 and 28-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 August 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/20/04,11/8/04,2/21/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner for your application in the USPTO has changed. Examiner Nathan Schlientz can be reached at 571-272-9924.

Status of Claims

Claims 14, 27 and 60 have been withdrawn in an Amendment filed 21 February 2007. As a result, Claims 1-13, 15-26 and 28-59 are examined herein on the merits for patentability. No claim is allowed at this time.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claims 1-13, 15-26 and 28-59 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 21-24 of copending Application No. 11/283,276 (hereinafter the conflicting Toth '276 application).

More specifically, claims 1-13, 15-26 and 28-59 of the instant application are directed to a stable mixture of crystalline polymorph Form I and Form II of desloratadine and a pharmaceutical formulation comprising said stable mixture and a pharmaceutically acceptable excipient, wherein said stable mixture comprises: from about 20 wt.% to about 80 wt.% desloratadine Form I; from about 80 wt.% to about 20 wt.% desloratadine Form II; and said stable mixture is made by a process involving one or more organic solvents selected from the group consisting of: n-heptane; toluene; isopropanol; and mixtures thereof. Claims 14, 27 and 60 of the instant application are directed to a method of treating allergenic reactions in a mammal comprising administering said pharmaceutical formulation to said mammal.

Claims 21-24 of the conflicting Toth '276 application are directed to a mixture of crystalline polymorph Form I and Form II of desloratadine and a pharmaceutical formulation comprising said mixture, wherein said mixture comprises: from about 35 wt.% to about 82 wt.% desloratadine Form I; from about 65 wt.% to about 18 wt.% desloratadine Form II; and from about 50 ppm to about 4000 ppm of one or more organic solvents selected from the group consisting of: n-hexane; n-heptane; toluene; ethyl acetate; isobutyl acetate; butanol; isobutanol; chloroform; and mixtures thereof. Claim 25 of the conflicting Toth '276 application is directed to a method of treating

allergenic reactions in a mammal comprising administering said pharmaceutical formulation to said mammal.

However, while the conflicting Toth '276 application does not claim the physicochemical properties (i.e., melting temperature, stability, flowability, solubility, dissolution rate, and bioavailability) of said stable mixture, as claimed in claims 4-13, 17-26 and 31-36 of the instant application, it is well within the purview of the skilled artesian to measure the physicochemical properties of said stable mixture by measuring, for example, the melting temperature and resistance to polymorphic transformation, chemical degradation and decomposition that said stable mixture possesses. One of ordinary skill in the art at the time the instant application was filed would have been motivated to conduct routine experimentation in order to determine whether the physicochemical properties (i.e., melting temperature, stability, flowability, solubility, dissolution rate, and bioavailability) of said stable mixture, to be incorporated into a pharmaceutical formulation, are constant and thus exhibit batch-to-batch consistency and uniformity from a drug manufacturing and quality assurance perspective.

As a result, although claims 1-13, 15-26 and 28-59 of the instant application are not identical to claims 21-24 of the conflicting Toth '276 application, the aforementioned claims are not patentably distinct each from the other because said claims are substantially overlapping in scope, with respect to said organic solvents and said weight percent ranges and ratios of crystalline polymorph Form I and Form II of desloratadine, as discussed hereinabove, as discussed hereinabove.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

It should be mentioned however that while claims 14, 27 and 60 of the instant application are currently withdrawn from further consideration as being directed to a non-elected invention, in the event that the elected product claims are found allowable, the requirement for restriction between the elected product claims and the non-elected method of using claims will be withdrawn, and the rejoined method of using claims will be fully examined for patentability in accordance with 37 CFR 1.104 and *In re Ochiai*, 71 F.3d 1565, 37 USPQ2d 1127 fled. Cir. 1995). In the event of rejoinder, Applicants are advised that claims 14, 27 and 60 of the instant application would be provisionally rejected under the judicially created doctrine of non-statutory obviousness-type double patenting as being unpatentable over conflicting claim 25 of the conflicting Toth '276 application. This would be a provisional non-statutory double patenting rejection since conflicting claim 25 of the conflicting Toth '276 application have not yet in fact been patented and are substantially overlapping in scope (i.e., drawn to a method of treating allergenic reactions in a mammal comprising administering said pharmaceutical formulation to said mammal) to claims 14, 27 and 60 of the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1,148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 1-13, 15-26 and 28-59 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,506,767 (hereinafter the Schumacher '767 patent).

Claims 1-13, 15-26 and 28-59 of the instant application are directed to a stable mixture of crystalline polymorph Form I and Form II of desloratadine and a pharmaceutical formulation comprising said stable mixture and a pharmaceutically acceptable excipient, wherein said stable mixture comprises: from about 20 wt.% to about 80 wt.% desloratadine Form I; from about 80 wt.% to about 20 wt.% desloratadine Form II; and said stable mixture is made by a process involving one or more organic solvents selected from the group consisting of: n-heptane; toluene; isopropanol; and mixtures thereof. The pharmaceutical formulation of the instant application is useful for treating allergenic reactions in a mammal.

With respect to claims 1-3, 15, 16, 28-30, 37 and 49 of the instant application, the Schumacher '767 patent teaches a stable mixture of crystalline polymorph Form I and Form II of desloratadine and a pharmaceutical formulation comprising said stable mixture and a pharmaceutically acceptable excipient; wherein said stable mixture

comprises from about 1 wt.% to about 15 wt.% polymorph Form I of desloratadine and from about 99 wt.% to about 85 wt.% polymorph Form II of desloratadine; and wherein said stable mixture is made by a process involving one or more organic solvents selected from the group consisting of: n-hexane; ethyl acetate; and mixtures thereof (abstract; column 1, lines 9-50 and 64-66; column 2, lines 50-52 and 65-67; column 3, lines 53-67; column 4, lines 1-41; column 8, lines 51-67; column 9; column 10; column 11; column 12, lines 1-8; claims 1, 2, 7, 8, 9 and 14-16).

With respect to claims 1-13, 15-26 and 28-59 of the instant application, although the Schumacher '767 patent teaches a stable mixture comprising from about 1 wt.% to about 15 wt.% polymorph Form I of desloratadine and from about 99 wt.% to about 85 wt.% polymorph Form II of desloratadine (column 3, lines 60-65; claims 8, 9, 14 and 15), the Schumacher '767 patent does not explicitly teach the instantly claimed stable mixture comprising from about 35 wt.% to about 82 wt.% polymorph Form I of desloratadine and from about 65 wt.% to about 18 wt.% polymorph Form II of desloratadine, wherein said stable mixture exhibits the instantly claimed melting temperature and stability (i.e., resistance to polymorphic transformation, chemical degradation and decomposition).

However, while the Schumacher '767 patent does not explicitly teach the instantly claimed weight percent ranges and ratios of polymorph Form I to Form II of desloratadine present within said stable mixture, the Schumacher '767 patent teaches that various solvent systems comprising a plurality of different organic solvents, which are routinely utilized by those of ordinary skill in the chemical, medicinal and

pharmaceutical arts for synthesis and purification (i.e., recrystallization) purposes, yielded various stable mixtures containing respective ratios of polymorph Form I to Form II of desloratadine (column 4, lines 12-41). In addition, while the Schumacher '767 patent does not explicitly teach the instantly claimed melting temperature and stability of said stable mixture; the Schumacher '767 patent teaches that said stable mixtures are suitable for incorporation into pharmaceutical formulations that meet the Good Manufacturing Practice (GMP) requirements of the Food and Drug Administration (FDA), thereby directly indicating that said stable mixtures and pharmaceutical formulations comprising said stable mixtures possess constant physicochemical properties, such as melting temperature and resistance to polymorphic transformation, chemical degradation and decomposition (column 1, lines 34-41; column 3, lines 60-65; column 4, lines 12-41; claims 8, 9, 14 and 15).

It is well within the purview of the skilled artesian to determine the optimal solvent system comprising a single specific organic solvent or a particular organic solvent/anti-solvent stable mixture for utilization in synthesizing and/or recrystallizing a stable mixture having a desired weight percent range and ratio of polymorph Form I to Form II of desloratadine. It is also well within the purview of the skilled artesian to measure the physicochemical properties of said stable mixture by measuring, for example, the melting temperature and resistance to polymorphic transformation, chemical degradation and decomposition that said stable mixture possesses. One of ordinary skill in the art at the time the instant application was filed would have been motivated to conduct routine experimentation in order to determine an optimal solvent system that is

particularly useful for obtaining, on a routine and reproducible basis, a stable mixture having a consistent desired weight percent range and ratio of polymorph Form I to Form II of desloratadine, so that the physicochemical properties (i.e., melting temperature, stability, flowability, solubility, dissolution rate, and bioavailability) of said stable mixture, to be incorporated into a pharmaceutical formulation, are constant and thus exhibit batch-to-batch consistency and uniformity from a drug manufacturing and quality assurance perspective. The Schumacher '767 patent further teaches that not only are each of polymorphs Form I and Form II of desloratadine independently useful for treating allergic reactions in mammals upon individual incorporation into a pharmaceutical formulation, but also stable mixtures containing respective weight percent ranges and ratios of polymorph Form I to Form II of desloratadine upon combined incorporation into a pharmaceutical formulation are also useful for treating allergic reactions in mammals, as instantly claimed (abstract; column 3, lines 60-65; claims 8, 9, 14 and 15).

Merely changing the form, purity, or another characteristic of an old product, the utility remaining the same as that of the old product, does not render the claimed product patentable. *Ex parte Hartop*, 139 USPQ 525 (Bd. App. 1962). However, the principle of law enunciated in *Ex parte Hartop* has been substantially discredited in *In re Cofer*, 354 F.2d 664, 667-668, 148 USPQ 268, 270-271 (CCPA 1966). Factors to be considered in determining whether a purified form of an old product is obvious over the prior art include: whether the instantly claimed chemical compound or composition has the same utility as closely related chemical compounds or compositions in the prior art;

and whether the prior art reasonably suggests either the particular form or structure of the instantly claimed chemical compound or composition, or suitable methods of obtaining that particular form or structure of the instantly claimed chemical compound or composition. See e.g., MPEP § 2144.04, and *In re Cofer*, 354 F.2d 664, 667-668, 148 USPQ 268, 270-271 (CCPA 1966) (Claims to the free-flowing crystalline form of a compound were held unobvious over references disclosing the viscous liquid form of the same compound because the prior art of record did not suggest the claimed compound in crystalline form or how to obtain such crystals.). "Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." See *In re Aller*, 105 USPQ 233,235 (CCPA 1955). "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages." See *Peterson*, 65 USPQ2d 1379, 1382 (Fed. Cir. 2003). "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose ... [T]he idea of combining them flows logically from their having been individually taught in the prior art." See e.g., MPEP § 2144.06 and *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Response to Arguments

Applicant's Remarks filed 21 February 2007 have been fully considered but they are not persuasive.

Applicants' argue in the aforementioned Remarks that the Schumacher '767 publication does not disclosed the instantly claimed ratios. However, Applicants' agree that the Schumacher '767 publication discloses both polymorph Form I and Form II of desloratadine as pharmaceutical agents for treating allergenic reactions (page 11 of the Remarks).

As mentioned above, It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose ... [T]he idea of combining them flows logically from their having been individually taught in the prior art. See e.g., MPEP § 2144.06 and *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Applicants' argue on page 13 that the Schumacher '767 publication discloses that it is undesirable to administer desloratadine to a mammal unless it is in a form that is pure as that disclosed in the Schumacher '767 patent, and that it can be inferred that it is unacceptable to have crystalline desloratadine that is not in as pure a form as possible, because the crystalline material would not have constant physical properties. However, the examiner respectfully disagrees. The Schumacher '767 publication discloses that "a mixture could lead to ***production*** of a descarbonylethoxyloratadine product which would exist as a variable mixture of variable composition having variable

physical properties." The Schumacher '767 publication teaches that variable properties in the production of the pharmaceutical would be unacceptable, not administering a mixture of Form I and Form II of desloratadine. As a matter of fact, the Schumacher '767 publication affords for a mixture of Form I and Form II of desloratadine to be administered as a pharmaceutical because the definition of "polymorph form 2 substantially free of polymorph form 1... means that the descarbonylethoxyloratadine polymorph form 2... contains less that about 15%, preferably less than about 10%, and more preferably less than about 5-8% of form 1..." (column 3, lines 60-67).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nathan W. Schlientz whose telephone number is 571-272-9924. The examiner can normally be reached on 8:30 AM to 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nathan W. Schlientz
Patent Examiner
Technology Center 1600
Group Art Unit 1616

Johann R. Richter
Supervisory Patent Examiner
Technology Center 1600
Group Art Unit 1616